DIAGNOSTIC UTILITY OF GGT AS A DIFFERENTIATOR OF HEPATIC OR BONE SOURCE OF RAISED ALP

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Introduction

Increased liver disease prevalence could be offset by earlier detection and intervention. Advancements have been made towards improved, automated, algorithm-driven testing pathways, (i.e. intelligent liver function testing (iLFT)); with the aim of increasing early diagnosis in a cost-effective manner. Individual Liver function tests (LFTs) (Total Protein, Albumin, Bilirubin, Alanine aminotransferase (ALT), Aspartate aminotransferase (AST) and Gamma-Glutamyl Transferase (GGT) are frequently requested in the routine laboratory. The clinical utility of GGT remains debated.[1]

Current liver profiles vary between laboratories (recent survey demonstrated that 25% of laboratories in the Republic of Ireland do not include GGT in the liver profile panel). However, inclusion of GGT is recommended by the Chemical Pathology Working Group, 2019.[2] It is considered helpful in determining the origin of a raised ALP but ALP isoenzyme fractionation, remains the Reference, [Gold Standard] method. In health, the majority of plasma Alkaline Phosphatase (ALP) is derived from bone and liver with small proportions from the intestine. In the later half of pregnancy, ALP of placental origin may enter the plasma.[3]

A study in 2008 concluded that a "raised GGT is a poor marker for predicting raised liver ALP isoenzymes" with a reported sensitivity and specificity of 76% and 52% respectively.[3] The latter appears to be an understudied area.

Aim

- To investigate the sensitivity and specificity of GGT in determining the isoenzyme(s) contributing to ALP elevations

Methodology

Retrospective Study

July 1997 – March 2019

Data Collection

1. Raised Total ALP Levels + all GGT levels (Beckman pre 2011, Abbott post 2011)

2. ALP Fractionation Studies Electrophoresis, *(Hydrasys 2 Sebia)*

Data Analysis

Interpretation of GGT results *(method & gender-specific RR)*

Interpretative reports of ALP Isoenzyme studies used to assess GGT diagnostic accuracy

Statistical Analysis

Descriptive statistics: categorical variables presented by percentages

Diagnostic GGT Test Evaluation (use of *2 X 2 Table*)

Inclusion Criteria:

- *All ALP isoenzyme(s) requested within the study period were eligible for inclusion.*

Exclusion Criteria:

- *Participants with no GGT/ALP level or Isoenzyme interpretative comment available*
- *Participants who had an ALP level within reference*
- *Participants whose gender* was not available (needed for cohort reviewed against gender-specific RR only)*

Study Flow

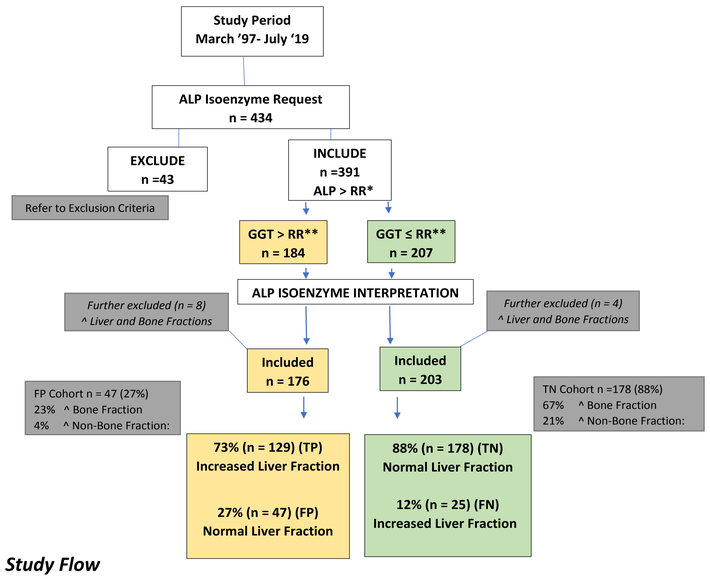

Figure 1. Study Flow

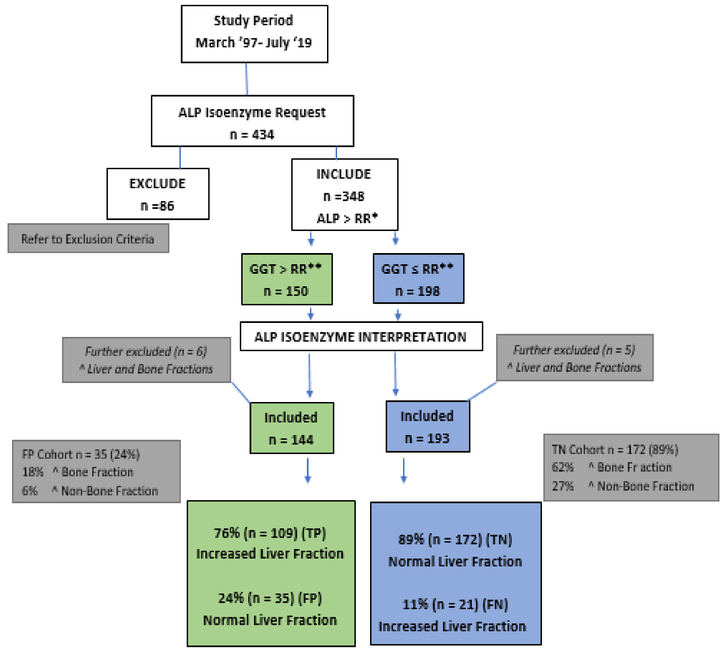

Figure 2. Study Flow: Application of gender-specific Reference range

RR = Reference Range; ALP= Alkaline Phosphatase RR = 30 – 130IU/L; GGT= Gamma- Glutamyl Transferase unisex RR > 40 IU/L (PRE 2011) >53 IU/L (POST 2011) Gender specific RR (Post 2011 GGT 8-53 IU/L** (Female), 11 – 67 IU/L** (Male) MMUH Locally derived (Lee et al. 2017)[4]*

Results

Table 1. Diagnostic GGT Test evaluation using 2 x 2 table

		ALP ISOENZYME FRACTIONATION (Electrophoresis)	
		Increased Liver Fraction	Normal Liver Fraction
Test Result	GGT > RR	TP = 129	FP = 47
	GGT ≤ RR	FN = 25	TN = 178
		Sensitivity (%) = 84 (PPV = 73 %)	Specificity (%) = 79 (NPV 88%)

Table 2. Diagnostic GGT Test evaluation using 2 x 2 table, Application of gender specific RR

		ALP ISOENZYME FRACTIONATION (Electrophoresis)	
		Increased Liver Fraction	Normal Liver Fraction
Test Result	GGT > RR	TP = 109	FP = 35
	GGT ≤ RR	FN = 21	TN = 172
		Sensitivity (%) = 84 (PPV = 76 %)	Specificity (%) = 83 (NPV 89%)

Table 3. GGT levels demonstrating 100% specificity/sensitivity

Increased Liver Fraction	100% SPECIFICITY	100% SENSITIVITY
GGT VALUE	>500IU/L	<13IU/L

Discussion & Conclusion

This large retrospective study (over 21y data) enhances the knowledge regarding diagnostic performance and limitations of GGT in predicting the source of ALP elevation. It supports earlier reports (1y study) regarding sensitivity (84% vs 76%) though we show higher specificity, especially when using GGT gender specific reference ranges (79% vs 52%).[3]

A GGT approximately 10 times the upper reference limit was highly predictive of ALP elevations due to increased liver ALP fractions. This study offers the potential to inform practice, including interpretative advice to clinicians.

References

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3. Al-Mossawi MH, Shine B. The role of gamma-glutamyl transpeptidase in screening requests for alkaline phosphatase isoenzymes. Ann Clin Biochem 2008; 45:35
4. Lee, G. R., Griffin, A., Halton, K., & Fitzgibbon, M. C. (2017). Generating method-specific Reference Ranges - A harmonious outcome?. Practical laboratory medicine, 2017; 9:1–11